UNITEDD STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

BOEHRINGER INGELHEIM PHARMACEUTICALS, INC., ET AL. *Plaintiffs*, v. HEC PHARM CO., LTD., ET AL. *Defendants*.	)	Civil Action No: 15-cv-5982 (PGS)(TJB) **OPINION**

SHERIDAN, U.S.D.J.

This matter comes before the Court on Defendants' motion to dismiss (ECF 328) the claims 10-17, 24 and 25 of infringement of the U.S. Pat. 8,853,156 (hereinafter "the '156 patent") pursuant to Fed. R. Civ. P. 12(c). The '156 patent identifies metformin as an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes mellitus. However, the '156 patent notes that patients who are adversely impacted or intolerable to metformin treatment (elderly and diabetic patients) generally experience several adverse symptoms, such as, decreased renal function, hypoglycemia, weight gain, edema, bone fracture, gastrointestinal side effects, heart failure and/or cardiac effects (hereinafter "targeted patient population").

The '156 patent generally concerns with the issue of decreased renal function because of metformin largely being excreted through the kidneys, and this issue requires careful monitoring and dosage regulation when treating elderly patients in the targeted patient population. In order to address this issue, the '156 patent discloses a pharmaceutical drug (DPP-IV inhibitor), which is mainly excreted via the liver and only to a minor extent via the kidney. As such, the monitoring of the targeted patient population is not necessary.

Defendants' allege that the aforementioned claims are patent ineligible because the claims recite a natural law that is based on pharmacokinetic observations of diabetic patients. As such, Defendants' move to dismiss the cited claims of infringement because they are invalid under 35 U.S.C. § 101.

In contrast, Plaintiffs' argue the motion should be denied because—(i) claims of the '156 patent are directed towards methods of treating the targeted patient population with metabolic diseases using non-naturally existing compounds, namely, DPP-IV inhibitors, which alter the natural state of the body in a new and useful way, and hence do not fall within the natural phenomena exception; (ii) there are factual disputes concerning the understanding of a person skilled in the art regarding DPP-IV inhibitors; and (iii) the patent eligibility challenge to the '156 patent is procedurally barred because Defendants failed to disclose their § 101 defense.

After a careful consideration of the briefs and oral arguments, the Court grants Defendants' motion to dismiss the claims 10-17, 24 and 25 of infringement of the '156 patent as being directed to patent ineligible subject matter for the reasons set forth below.

The '156 Patent

The inventive concepts disclosed in the '156 patent relate to the use of DPP-IV inhibitors for treating and/or preventing metabolic diseases, particularly diabetes (especially type 2 diabetes mellitus), in the targeted patient population. (*See* the '156 patent, col. 1, ll. 5-10; col. 9, ll. 30-45). The Court notes that the '156 patent includes a total of twenty-five (25) claims, wherein claims 1, 23, 24 and 25 are in independent form.

Conventional antidiabetic or antihyperglycemic agents used for treating blood sugar levels include, metformin, sulphonylureas, thiazolidinediones, glinides, alpha-glucosidase blockers, GLP-1 and GLP-1 analogues, as well as insulin and insulin analogues. However, these

conventional antidiabetic agents have various side effects such as lactic acidosis or gastrointestinal side effects; hypoglycemia or weight gain; edema, bone fracture, weight gain or heart failure; and gastrointestinal adverse effects. (*Id.* at col. 1, ll. 35-50).

With respect to treatment with metformin, adverse symptoms include gastrointestinal side effects or lactic acidosis, which may lead to decreased renal function. As such, metformin therapy can be inappropriate for the targeted patient population. (*Id.* at col. 1, ll. 55-67). Accordingly, the inventive concepts disclosed in the '156 patent are directed towards disclosing a pharmaceutical drug, which is mainly excreted via the liver and only to a minor extent via the kidney. (*Id.* at col. 3, ll. 10-15; col. 23, ll. 1-10).

The '156 patent further discloses that DPP-IV inhibitors interfere with the plasma level of bioactive peptides, including the peptide GLP-1; and are considered to be promising drugs for the treatment of diabetes mellitus. The uses of DPP-IV inhibitors in metabolic (especially diabetic) diseases are disclosed in numerous references as discussed in col. 4, ll. 15-25 of the '156 patent. The drugs belonging to the DPP-IV inhibitor class include, Sitagliptin, Vildagliptin, Saxagliptin and Alogliptin. The '156 patent discusses the different structural formulations of the aforementioned drugs, the patent(s) and/or publications in which they are disclosed, the specific salts of the aforementioned drugs, and their formulation. (*Id.* at col. 4, ll. 25—col. 9, ll. 30).

The '156 patent further discloses that the DPP-IV inhibitors may be combined with one or more conventional antihyperglycemic agents selected from sulphonylureas, thiazolidinediones (e.g. pioglitazone), glinides, alpha-glucosidase blockers, GLP-1 and GLP-1 analogues, and insulin and insulin analogues, for use in (first line) therapy of type 2 diabetes patients for the targeted patient population. (*Id.* at col. 12, ll. 27-35).

According to the inventive concepts of the '156 patent, the DPP-IV inhibitor may be an oral DPP-IV inhibitor, whose active metabolites have a wide therapeutic window, and that are eliminated via hepatic metabolism or biliary excretion. The DPP-IV inhibitor of the '156 patent is substantially or mainly excreted via the liver for which renal excretion represents no substantial or only a minor elimination pathway. (*Id.* at col. 13, ll. 40-50). The DPP-IV inhibitors disclosed in various embodiments in cols. 15, 16, 17, 18 and 19 of the '156 patent allegedly improve on the conventional DPP-IV inhibitors by combining exceptional potency and a long-lasting effect with (i) favorable pharmacological properties, (ii) receptor selectivity and (iii) a favorable side effect profile, or bringing about unexpected therapeutic advantages, or improvements when combined with other pharmaceutical active substances. (*Id.* at col. 19, ll. 30-35).

In a preferred embodiment (embodiment A), the '156 patent discloses that DPP-IV inhibitors can be prepared using synthetic methods as described in the literature. The purine derivatives of formula (I) can be obtained as described in various disclosures. (*Id.* at col. 19, ll. 50-65). As such, the pharmaceutical compositions, according to the invention disclosed in the '156 patent comprising the DPP-IV inhibitors, are prepared by the skilled person using pharmaceutically acceptable formulation excipients as described in the art. (*Id.* at col. 20, ll. 30-35).

With respect to administering the DPP-IV inhibitors to a patient, according to preferred embodiment A of the DPP-IV inhibitors, the '156 patent discloses that the dosage typically required of the DPP-IV inhibitors, when administered intravenously, is 0.1 mg (milligram) to 10 mg, preferably 0.25 mg to 5 mg, for a duration of one (1) to four (4) times a day. (*Id.* at col. 21, ll. 20-25).

A preferred example of DPP-IV inhibitor disclosed in the '156 patent is the BI 1356 inhibitor.[1] The BI 1356 "exhibits high potency, 24 h [hour] duration of action, and a wide therapeutic window." According to the '156 patent, patients with type 2 diabetes receiving multiple oral doses of 1, 2.5, 5 or 10 mg of BI 1356, once daily for twelve (12) days, show favorable pharmacodynamics and pharmacokinetic profile (shown in Table 1, col. 23, ll. 15-35) with rapid attainment of steady state. (*Id.* at col. 22, ll. 40-50). BI 1356 is mainly excreted via the liver and only to a minor extent via the kidney. The fraction of BI 1356 eliminated via the kidneys increases very slightly over time. The non-renal elimination of BI 1356 in combination with its low accumulation potential and broad safety margin may be of significant benefit to the targeted patient population. (*Id.* at col. 23, ll. 1-10).

The '156 patent further discloses that the drugs belonging to the DPP-IV inhibitor class (i.e., Sitagliptin, Vildagliptin, Saxagliptin and Alogliptin) may be used in conjunction with other active substances such that improved treatment results can be obtained. The active substances which may be obtained commercially as pharmaceutical compositions are described in numerous places in the prior art, for example, the "Rote Liste®" of the federal association of pharmaceutical industry, or in the annual "Physicians' Desk Reference." (*Id.* at col. 23, ll. 60—col. 24, ll. 2). The particular antidiabetic partner drugs, especially for patients with type 2 diabetes and renal impairment, for the combined use with the DPP-IV inhibitors may include, for example, glibenclamide, dlimepiride and gliquidon. (*Id.* at col. 25, ll. 45-50).

[1] *See* p. 6, left column of the '156 patent, "Other Publications" section, which disclose prior publications directed towards BI 1356. For example, Thomas, L, et al: "BI 1356, a novel and selective xanthine beased DPP-IV inhibitor, exhibits a superior profile when compared to sitagliptin and vildagliptin." Diabetologoa, vol. 50, No. Suppl. 1, Sep. 2007, p. S363.

Declaration of Dr. Utpal Pajvani

Dr. Pajvani, on behalf of Plaintiffs, provides a declaration in support of Plaintiffs' memorandum of law in opposition to Defendants' Rule 12(c) motion to dismiss the claims 10-17, 24 and 25 of infringement of the '156 patent. (*See* Dr. Utpal Pajvani's Declaration ("Pajvani Decl."), ECF 354-1).

Dr. Pajvani recognizes that claims 10-17, which are asserted by Plaintiffs against Defendants, depend from independent claim 1, and as such claims 10-17 include all the limitations set forth in claim 1. (*See* Pajvani Decl. ¶ 15). In paragraphs 19 and 20 of Dr. Pajvani's declaration, Dr. Pajvani indicates that DPP-IV enzymes are the key players in a glycogenesis process (i.e., when the blood glucose level is high). That is, DPP-IV enzymes, which are found on the surface of the cells, rapidly inactivates or degrades the hormones—GLP-1 (glucagon-like peptide) and GIP (glucose-dependent insulotropic polypeptide)—which are responsible for the release of insulin, and as such depress the level of insulin in the body. (*See* Pajvani Decl. ¶ 21).

With respect to the inventive concepts recited in the '156 patent, in particular claims 10-17 and 24-25, Dr. Pajvani indicates that the aforementioned natural process is artificially modified in order to treat and/or prevent metabolic diseases. In particular, Dr. Pajvani notes that the DPP-IV inhibitors, which are synthetic compounds, bind to the DPP-IV enzymes that are on the surface of the cells in order to inactivate the DPP-IV enzymes. The DPP-IV enzymes are inhibited due to their inactivation. By inhibiting the DPP-IV enzymes, the half-life of GLP-1 and GIP hormones is artificially lengthened. The increased levels of GLP-1 and GIP hormones causes the pancreases to increase insulin secretion and decrease glucagon secretion, which in turn leads to decreased level of glucose in the blood. Accordingly, these series of reactions result in lowering blood glucose level in the body. (*See* Pajvani Decl. ¶ 22).

Unlike the DPP-IV inhibitors of the '156 patent, the DPP-IV inhibitors prior to the '156 patent, such as sitagliptin, saxagliptin, vildagliptin, and alogliptin, require dose adjustment for the targeted patient population. (*See* Pajvani Decl. ¶ 32). As such, like metformin, the aforementioned four DPP-IV inhibitors, require regular monitoring of kidney function, which is labor-intensive for the treating physician and often leads to a decreased adherence of regular monitoring of the targeted patient population. (*See* Pajvani Decl. ¶ 33, *citing* Exhibit F. Januvia Prescribing Information at 2; Exhibit G, Onglyza Prescribing Information at 2; Ex. H, Galvus Prescribing Information, 19; Exhibit I, Nesina Prescribing Information, at 2). Dr. Pajvani indicates that the since regular monitoring of the kidney functions for the targeted patient population, who are taking sitagliptin, saxagliptin, vildagliptin, and alogliptin, are at the very early stages of renal impairment, it is of particular importance because the targeted patient population will not have their medication dosage adequately adjusted, which may result in dangerous side effects. (*See* Pajvani Decl. ¶ 33).

According to Dr. Pajvani, unlike the conventional DPP-IV inhibitors, the inventive concepts disclosed in the '156 patent does not require dose adjustment in patients with any degree of renal impairment. (*See* Pajvani Decl. ¶ 35; *see also* Declaration of Dr. Pajvani in support of Plaintiffs' Opening Claim Construction Brief, ECF 349 at ¶ 16).

The Court recognizes the distinction of no dose adjustments required for the pharmaceutical drug disclosed in the '156 patent; however, the Court notes that the cited claims of infringement of the'156 patent do not claim dose adjustments to treat the targeted patient population. Instead, the cited claims of infringement further define the metabolic disorder, the specific contraindication experienced by the targeted patient population, and the processing of the DPP-IV inhibitors by the human body upon ingestion of the same. As such, the inventive concepts of the '156 patent not requiring dose adjustment is not an issue in the cited claims of infringement.

Fed. R. Civ. P. 12(c)

Rule 12(c) of the Federal Rules of Civil Procedure permits a party to dismiss a suit "[a]fter the pleadings are closed...but early enough not to delay trial." Fed. R. Civ. P. 12(c). For a complaint to survive dismissal, it "must contain sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'" *Wireless Media Innovations, LLC v. Maher Terminals, LLC*, 100 F.Supp.3d 405 (D.N.J. April 20, 2015) (citing *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009)). In determining the sufficiency of a complaint, the Court must accept all well-pleaded factual allegations in the complaint as true and draw all reasonable inferences in favor of the nonmoving party. *Id.* (citing *Phillips v. County of Allegheny*, 515 F.3d 224, 234 (3d Cir.2008)).

A motion for judgment on the pleadings is "functionally identical" to a Rule 12(b)(6) motion to dismiss for failure to state a claim. *Cave Consulting Group, Inc. v. Truven Health Analytics, Inc.*, 2016 WL 283478, at *1 (N.D. Cal. Jan. 25, 2016) (citing *Dworkin v. Hustler Magazine, Inc.*, 867 F.2d 1188, 1192 (9th Cir. 1989)); (*Affinity Labs of Texas, LLC v. Amazon.Com, Inc.*, 2015 WL 3757497 (W.D. Tx. June 12, 2015) (citing *Doe v. MySpace, Inc.*, 528 F.3d 413, 418 (5th Cir. 2008)). The Court must accept "all factual allegations in the complaint as true and construe them in light most favorable to the non-moving party." *Id.* (internal citations omitted).

(I)

In order to consider Defendants' motion to dismiss the claims of infringement of the '156 patent under Rule 12(c) (ECF 328), the Court must first determine whether claim construction is necessary.

In recent years, precedent holds that courts may properly decide the question of patent eligibility at the pleading stage and without first construing the claim terms. *Wireless Media*, 100 F.Supp.3d at 410 (citing *Bancorp Servs., L.L.C. v. Sun Life Assur. Co. of Canada (U.S.)*, 687 F.3d

1266, 1273 (Fed. Cir. 2012) ("[C]laim construction is not an inviolable prerequisite to a validity determination under § 101.")) Where appropriate, district courts have adjudicated subject matter eligibility before claim construction. *Id.* The Courts have indeed dismissed patent suits on the pleadings because the patents were ineligible under § 101. *Id.* (citing *Lumen View Tech. LLC v. Findthebest.com, Inc.*, 984 F.Supp.2d 189, 205 (S.D.N.Y. 2013) (granting judgment on the pleadings because "[t]he claimed process elements of Claim 1 are straightforward.").

A motion challenging validity of a patent under 35 U.S.C. § 101 may be brought at the motion to dismiss stage. *Eagle View Technologies, Inc. v. Xactware Solutions, Inc.*, 2016 WL 4154136 (D.N.J. Aug. 2016) (citing *Ultramercial, Inc. v. Hulu, LLC*, 772 F.3d 709, 717 (Fed. Cir. 2014) (affirming district court's invalidity ruling on a motion to dismiss)). "Although the determination of patent eligibility requires a full understanding of the basic character of the claimed subject matter, claim construction is not an inviolable perquisite to a validity determination under § 101." *Content Extraction & Transmission LLC v. Wells Fargo Bank, Nat'l Ass'n*, 776 F.3d 1343, 1349 (Fed. Cir. 2014) (citations omitted). But, "it will ordinarily be desirable—and often necessary—to resolve claim construction disputes prior to a § 101 analysis." *Bancorp Servs., L.L.C. v. Sun Life Ass. Co. of Can. (U.S.*), 687 F.3d 1266, 1273 (Fed. Cir. 2012).

Although claim construction of the '156 patent has not been conducted, there has been sufficient briefing that the Court "[understands] the basic character of the claimed subject matter," to determine Defendants' motion to dismiss the claims of infringement of the '156 patent on the pleadings. *Eagle View*, 2016 WL 415413, at *2 ("Although the determination of patent eligibility requires a full understanding of the basic character of the claimed subject matter, claim construction is not an inviolable perquisite to a validity determination under § 101") (internal citations omitted).

(II)(A)

For purposes of determining patent eligibility of the claims of infringement of the '156 patent, the Court limits its review and analysis to claims 10-17 and 24-25 because only these aforementioned claims have been asserted for infringement against Defendants. (*See* Defs.' Br. at 3, fn. 4, ECF 331). Since Boehringer narrowed its asserted claims after the pleadings were closed, we are limiting our decision only to these claims of the '156 patent.

The statute, 35 U.S.C. § 101, provides that patents may only issue for "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." However, the Supreme Court "ha[s] long held that this provision contains an important implicit exceptions: Laws of nature, natural phenomena, and abstract ideas [which] are not patentable." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S.Ct. 2347, 2354 (2014) (quoting *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S.Ct. 2107, 2116 (2013)) (internal quotations omitted). As explained by the Supreme Court, "the concern that drives this exclusionary principle [is] one of pre-emption." *Id.* (citations omitted). "The ultimate question of patent eligibility under § 101 is an issue of law." *In re BRCA1—and BRCA2—Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 759 (Fed. Cir. 2014).

In evaluating whether a patent claim recites patent eligible subject matter under 35 U.S.C. § 101, the Court undertakes a two-step inquiry to determine: (1) whether the claims at issue are directed to a patent ineligible concept (i.e., law of nature, natural phenomena, or abstract idea); and (2) if so, then the Court must determine whether the "claim's elements, considered both individually and 'as an ordered combination,' 'transform the nature of the claim' into a patent-eligible application." *Alice*, 134 S.Ct. at 2355 (quoting *Mayo Collaborative Servs. v. Prometheus*

Labs., Inc., 132 S.Ct. 1289, 1297–98 (2012)). Step two of this analysis is a search for an "inventive concept." *Id.* (quoting *Mayo*, 132 S.Ct. at 1294).

The abstract-idea exception precludes patents that "would pre-empt use of [a particular] approach in all fields, and would effectively grant a monopoly over an abstract idea." *Bilski v. Kappos*, 130 S.Ct. 3218, 3231 (2010). For example, "[a] mathematical formula as such is not accorded the protection of our patent laws, and this principle cannot be circumvented by attempting to limit the use of the formula to a particular technological environment." *Diamond v. Diehr*, 450 U.S. 175, 184 (1981) (citations omitted). "[M]ethods which can be performed mentally, or which are the equivalent of human mental work, are unpatentable abstract ideas." *CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1371 (Fed. Cir. 2011).

With respect to what constitutes an "abstract idea," the Court in *Alice* noted that the "abstract ideas" category is one that embodies the "longstanding rule that '[a]n idea of itself is not patentable." *Id.* at 2355 (*citing Le Roy v. Tatham*, 14 How. 156, 175 (1852) ("A principle, in the abstract, is a fundamental truth; an original cause; a motive; these cannot be patented, as no one can claim in either of them an exclusive right")). However, the Court also indicated that it need not "labor to delimit the precise contours of the 'abstract ideas' category in this case." *Id.* at 2357; *also see Enfish, LLC v. Microsoft Corp.*, 822 F.3d 1327, 1334.

In contrast, "an application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection." *Diehr*, 450 U.S. 175, 187. The law of nature or natural phenomena exception precludes patents directed towards phenomena of nature, mental processes, and abstract intellectual concepts, as they are "basic tools of scientific and technological work." *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972). For example, "sets of steps conducted entirely by nature are not subject to patenting since they are not invented by man; sets

of steps occurring only in the mind are not subject to patenting because mental processes are but disembodied thoughts, whereas inventions which Congress is constitutionally empowered to make patentable are tangible embodiments of ideas in useful or technological arts." *In re Sarkar*, 588 F.2d 1330, 1333 (CCPA 1978). "The discovery of a law of nature cannot form [the] basis of [a] patent." *Armour Pharmaceutical Co. v. Richardson-Merrell, Inc.*, 396 F.2d 72 (3d Cir. 1968).

Instead, the "[p]atented process that focuses upon use of natural law must also contain other elements or combination of elements, sometimes referred to as 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Mayo*, 132 S.Ct. 1289, 1294. An application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection. *Diehr*, 450 U.S. 175, 187-188 (internal citations omitted).

The Supreme Court precedents on the issue of what constitutes patent eligibility have stated that patent claims directed to an abstract idea, a law of nature, or a natural phenomenon are patent ineligible under § 101. For example, in *Benson* the Supreme Court held that an algorithm, or mathematical formula, is like a law of nature, which cannot be the subject of a patent (*see Benson*, 409 U.S. 63 at 71); and in *Parker v. Flook*, the Court held that processes using mathematical formulas that, like laws of nature, are not themselves patentable (*see Parker*, 437 U.S. 584, 590-591 (1978)). Thereafter, about thirty-years later, in *Bilski*, the Supreme Court found that the claimed invention that explained how buyers and sellers of commodities in the energy market could protect, or hedge, against the risk of price changes and that reduced this concept of hedging to a mathematical formula was an abstract idea, and thus was not a patentable process (*see Bilski*, 130 S.Ct. at 3229); and in *Mayo* the Supreme Court held that "[the] [p]henomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are

the basic tools of scientific and technological work" (*see Mayo*, 132 S.Ct. at 1293). Lastly, more recently, the Supreme Court in *Alice* held that "claims in patents for mitigating settlement risk in financial transactions by using a computer system as a third-party intermediary were directed to a patent-ineligible concept" (*see Alice*, 134 S.Ct. 2347, 2355).

The Supreme Court has also indicated that patent claims directed to an abstract idea, a law of nature, or a natural phenomenon, can be found to be patent eligible if the claims recite additional claim limitations or features that add "significantly more" to the alleged abstract idea, law of nature, or natural phenomenon such that the claim is transformed into a patent eligible subject matter. For example, in *Diehr* the Supreme Court held that the overall process was patent eligible because of the way the additional steps of the process integrated the equation into the process as a whole (*see Diehr*, 450 U.S. 175 at 187); and in *Diamond v. Chakrabarty*, the Court held that a human-made bacterium with markedly different characteristics from any found in nature, and one having the potential for significant utility, was considered patentable subject matter, and not nature's handiwork (*see Diamond v. Chakrabarty*, 447 U.S. 303, 310 (1980)).

The first prong of the *Mayo/Alice* two step inquiry for determining patent ineligibility was further clarified by the Federal Circuit in *Enfish*. The Court in *Enfish* stated that the "directed to" inquiry "applies a stage-one filter to claims, considered in light of the specification, based on whether 'their character as a whole is directed to excluded subject matter.'" *Enfish*, 822 F.3d at 1335 (*citing Internet Patents Corp. v. Active Network, Inc.*, 790 F.3d 1343, 1346 (Fed. Cir. 2015); *also see Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369, 1375, 2016 WL 1393573, at *5 (Fed.Cir.2016) (inquiring into "the focus of the claimed advance over the prior art")). As such, the Federal Circuit in *Enfish* indicated that the first prong of the *Mayo/Alice* two-step inquiry requires

determining whether the focus of the claims, in light of the specification, is on a specific asserted 'improvement' in that particular technological area. *Id.* at 1335.[2]

The Court in *Enfish* cautioned that when determining whether claims are directed to patent eligible subject matter, they should not be "described at a 'high level' of abstraction and untethered from the language of the claims because doing so ensures that exceptions to 35 U.S.C. § 101 will swallow the rule." *Id.* at 1337 (*citing Alice*, 134 S.Ct. at 2354). The *Enfish* Court noted that "we tread carefully in construing this exclusionary principle [of laws of nature, natural phenomena, and abstract ideas] lest it swallow all of patent law." *Id.* Likewise, the Supreme Court also cautioned that over generalizing claims, "if carried to its extreme, make[s] all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious." *Diehr*, 450 U.S. at 189, n. 12.

Here, we begin with step one—determining whether claims 10-17 of the '156 patent are "directed to" a patent ineligible concept. First, the Court considers independent claim 1 because claims 10-17 depend from claim 1. (*See* Manual of Patent Examining Procedure ("MPEP") § 608.01(n); 35 U.S.C. 112 (d)[3]). Claims 10-17 are in dependent form because they relate back to claim 1, as noted from their respective preamble. Claim 1 of the '156 patent recites:

[2] *See Enfish*, 822 F.3d at 1335 ("We thus see no reason to conclude that all claims directed to improvements in computer-related technology, including those directed to software, are abstract and necessarily analyzed at the second step of *Alice*, nor do we believe that *Alice* so directs. Therefore, we find it relevant to ask whether the claims are directed to an improvement to computer functionality versus being directed to an abstract idea, even at the first step of the *Alice* analysis").

[3] 35 U.S.C. 112 (d): "Subject to subsection (e), a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers."

> A method of treating and/or preventing metabolic diseases in a patient for whom metformin therapy is inappropriate due to at least one contraindication against metformin comprising
>
> orally administering to the patient a DPP-IV inhibitor wherein the contraindication is selected from the group consisting of: renal disease, renal impairment or renal dysfunction, unstable or acute congestive heart failure, acute or chronic metabolic acidosis, and hereditary galactose intolerance.

(col. 29, ll. 2-12 of the '156 patent). Claim 1 is a method claim, with a preamble that recites, "treating and/or preventing metabolic diseases in a patient for whom metformin therapy is inappropriate due to at least one contraindication against metformin." The preamble is followed by the transitional phrase of "comprising."[4] The transitional phrase is followed by the body of the claim, which includes—(i) the step of "orally administering to the patient a DPP-IV inhibitor;" and (ii) a Markush group[5] following a wherein clause that further defines the different types of contraindications associated with metformin therapy. The end result is to treat a targeted patient population with a DPP-IV inhibitor.

Defendants' assert in their briefs that the claims of the '156 patent are patent ineligible because they recite a natural law that are essentially directed to pharmacokinetic observations of diabetic patients. (*See* Defs.' Br. at 5-14, ECF 331). In contrast, Plaintiffs' assert that the claims of the '156 patent are patent eligible because they recite methods of using non-naturally existing compounds, namely DPP-IV inhibitors, which alter the natural state of the body in a new and

[4] *See* MPEP § 2111.03 "Transitional Phrases" ("The transitional term "comprising", which is synonymous with 'including,' 'containing,' or 'characterized by,' is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.").

[5] *See* MPEP § 2173.05(h) "Alternative Limitations—Markush Groups" (A 'Markush' claim recites a list of alternatively useable species (internal citations omitted). A Markush claim is commonly formatted as: 'selected from the group consisting of A, B, and C;' however, the phrase 'Markush claim' means any claim that recites a list of alternatively useable species regardless of format.").

useful way. (*See* Pls.' Br. at 11-17, ECF 354). In support of their position, Plaintiffs' rely on the recent Federal Circuit case, *Rapid Litigation Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042 (Fed. Cir. July 5, 2016). The Court does not find Plaintiffs' arguments persuasive.

In *CellzDirect*, the Federal Circuit found the claims at issue to be directed to "a new and useful laboratory technique for preserving hepatocytes." *CellzDirect*, 827 F.3d at 1048. The Court noted that unlike the claims in recent cases that amounted to nothing more than observing or identifying the ineligible concept itself, the claims in the *CellzDirect* were immediately distinguishable. *Id.* (internal citations omitted). That is, the claims in *CellzDirect* recited detailed steps in the claims that achieved a better way of preserving the hepatocytes. In particular, the Court noted that "[b]ecause the claimed process involves both multiple freeze-thaw cycles and pooling cells from various donors, it results in a preparation that is both new and vastly more useful for research than hepatocyte preparations made by conventional methods." *Id.* at 1048-49. In other words, the claims at issue in *CellzDirect* required a series of steps such as—(i) subjecting hepatocytes that have frozen and thawed to separate viable hepatocytes from nonviable hepatocytes; (ii) recovering separated viable hepatocytes; (iii) cryopreserving the recovered viable hepatocytes to thereby form said desired preparation of hepatocytes; and (iv) resulting in a new and improved hepatocyte that was not disclosed in the conventional methods. *Id.* at 1046.

However, the claims in *CellzDirect* are not similar to the claims in the '156 patent. For example, claim 1 of the '156 patent only recites a single instruction of "orally administering" a DPP-IV inhibitor to the targeted patient population rather than a series of steps tied to tangible embodiments. In brief, claim 1 of the '156 patent provides no contribution over conventional knowledge of administering DPP-IV inhibitors.

The case of *Mayo* is more analogous to the claims at issue here. In *Mayo*, the Supreme Court found that "[c]laim 1 […] states that *if* the levels of 6–TG in the blood (of a patient who has taken a dose of a thiopurine drug) exceed about 400 pmol per $8x10^8$ red blood cells, *then* the administered dose is likely to produce toxic side effects. While it takes a human action (the administration of a thiopurine drug) to trigger a manifestation of this relation in a particular person, the relation itself exists […] apart from any human action." In *Mayo*, the Supreme Court noted that the relation between the blood levels and the thiopurine drug was a consequence of the ways where thiopurine compounds were metabolized by the body, which the Court determined to constitute "entirely natural processes." *Mayo*, 132 S.Ct. at 1296-97.

Similarly, here, claim 1 recites to, orally administer a DPP-IV inhibitor. Upon administering the DPP-IV inhibitor, the natural biological process in the human body operates to increase the insulin secretion. Thereby, decreasing the glucagon secretion and reducing the level of glucose in the blood. Subsequent thereto DPP-IV inhibitor is substantially or mainly excreted via the liver and only to a minor extent via the kidney (*See* Pajvani Decl. ¶ 22; the '156 patent, col. 13, ll. 40-50; col. 23, ll. 1-10).

The Court recognizes that Defendants' in their briefs, in reliance on *Mayo*, advance the position that the claims of the '156 patent are patent ineligible because they are directed to a natural law. (*See* Defs.' Br. at 5-14, ECF 331). However, the Court notes that unlike the claims in *Mayo*, which required administering a dose upon determining that certain levels in the blood were increased; claim 1 of the '156 patent, at its core, simply recites the act of 'administering' a DPP-IV inhibitor because it does not require any prior determination that natural body levels have changed or altered before performing the step of administering the DPP-IV inhibitor. As such, the act of administering the DPP-IV inhibitor to the targeted patient population, as noted in claim 1 of

the '156 patent, is an abstract idea. *See CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1371 (Fed.Cir.2011) ("[M]ethods which can be performed mentally, or which are the equivalent of human mental work, are unpatentable abstract ideas...."); *Mayo*, 132 S.Ct. at 1293 ("Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work.").

Additionally, pursuant to Federal Circuit's guidance in *Enfish* with respect to determining whether the focus of the claims, in light of the specification, is on a specific asserted 'improvement' in that particular technological area when determining what the claims are "directed to," the Court finds claim 1 of the '156 patent to be directed to an abstract idea. Here, the improvement over the conventional DPP-IV inhibitors is that the DPP-IV inhibitors disclosed in the '156 patent are mainly excreted via the liver, and only to a minor extent via the kidney, in order to treat the targeted patient population. As such, the monitoring of the targeted patient population is not necessary. However, the improvement of having the DPP-IV inhibitors excreted via the liver, instead of the kidney, is performed at the anatomical level of the human body, where a series of reactions in the human body process the DPP-IV inhibitor under the natural biological process. Accordingly, the Court finds that claim 1 of the '156 patent, which recites a single instruction of administering the DPP-IV inhibitor to the targeted patient population, is directed to an abstract idea.

(II)(B)

Now the Court turns to the second step of the *Mayo/Alice* framework to search for an "inventive concept." That is, the Court now determines whether the "claim's elements, considered both individually and 'as an ordered combination,' 'transform the nature of the claim' into a patent eligible application." *Alice*, 134 S.Ct. at 2355; *also see Mayo*, 132 S.Ct. at 1294 (The requirement for substantive claim limitations beyond the mere recitation of a disembodied fundamental concept

has "sometimes" been referred to as an "inventive concept") (internal citations omitted). The "inventive concept" equates to an element or a combination of elements, recited in the claim, which are "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Id.* (*citing Mayo*, 132 S.Ct. at 1294).

In *Ultramercial*, the Federal Circuit noted that the claim limitations must be examined to determine whether the claims contain an "inventive concept" to "transform" the claimed abstract idea into a patent eligible subject matter. *Ultramercial*, 772 F.3d at 715 (citing *Alice*, 134 S.Ct. at 2357). The transformation of an abstract idea into a patent eligible subject matter "requires more than simply stat[ing] the [abstract idea] while adding the words 'apply it.'" *Id.* (quoting *Mayo*, 132 S.Ct. at 1294). "A claim that recites an abstract idea must include 'additional features' to ensure 'that the [claim] is more than a drafting effort designed to monopolize the [abstract idea].'" *Id.* (quoting *Mayo*, 132 S.Ct. at 1297). Those "additional features" must be more than the "well-understood, routine, conventional activity." *Id.* (*citing Mayo*, 132 S.Ct. at 1298).

When analyzing the "additional features" as being more than well-understood, routine and conventional activity, the Federal Circuit in *Bascom* cautioned that such determination should not undertake an obviousness analysis under 35 U.S.C. § 103. *Bacsom Global Internet v. AT&T Mobility, LLC*, 827 F.3d 1341, 1350 (Fed. Cir. June 27, 2016) ("The district court's analysis in this case, however, looks similar to an obviousness analysis under 35 U.S.C. § 103, except lacking an explanation of a reason to combine the limitations as claimed. The inventive concept inquiry requires more than recognizing that each claim element, by itself, was known in the art. As is the case here, an inventive concept can be found in the non-conventional and non-generic arrangement of known, conventional pieces.").

Here, when considering claim 1 of the '156 patent as a whole, the Court finds that the additional features recited in claim 1 do not amount to "significantly more," which transform the abstract idea of administering the DPP-IV inhibitor to a patent eligible subject matter. That is, when considering the following additional features—(i) the preamble of claim 1, "treating and/or preventing metabolic diseases in a patient for whom metformin therapy is inappropriate due to at least one contraindication against metformin;" and (ii) the body of claim 1, "wherein the contraindication is selected from the group consisting of: renal disease, renal impairment or renal dysfunction, unstable or acute congestive heart failure, acute or chronic metabolic acidosis, and hereditary galactose intolerance"—in conjunction with "orally administering to the patient a DPP-IV inhibitor," as recited in claim 1, the Court finds that these additional features recite well-understood, routine, and conventional activity that do not transform the abstract idea into an 'inventive concept.'

For example, with respect to the preamble and the wherein clause recited in the body of claim 1, the '156 patent discloses, "Type 2 diabetes mellitus is a common disease of increasing prevalence worldwide and may be associated with […] microvascular complications such as […] and/or renal impairment or failure;" "metformin can be associated with lactic acidosis or gastrointestinal side effects […] [and] thiazolidinediones can be associated with edema, bone fracture, weight gain or heart failure/cardiac effects." (*See* the '156 patent, col. 1, ll. 20-25, 40-45). These disclosures indicate that the inventor of the '156 patent recognized that these aforementioned issues were known and well-understood in the scientific community. That is, it was known and well-understood in the medical community that the targeted patient population may experience renal impairment, congestive heart failure, and/or hereditary galactose intolerance. (*See Id.* at col. 12, ll. 27-35; *also see* Pajvani Decl. ¶ 15).

The Court notes that unlike the claims in *CellzDirect*, claim 1 of the '156 patent does not amount to significantly more than an abstract idea of providing an instruction for a medical care professional who is treating the targeted patient population. The instruction of claim 1 can be conducted via mental processes, which is not tied to any tangible embodiments. *In re Sarkar*, 588 F.2d at 1333 ("sets of steps occurring only in the mind are not subject to patenting because mental processes are but disembodied thoughts"); *Alice*, 134 S.Ct. at 2357 (*citing Mayo*, 132 S.Ct. at 1298 ("the process at issue amounted to 'nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients.'").

The only improvement over the conventional DPP-IV inhibitors (i.e., Sitagliptin, Vildagliptin, Saxagliptin and Alogliptin) (*see* the '156 patent, col. 22, ll. 1-25; col. 23, ll. 60—col. 24, ll. 2) being that the DPP-IV inhibitor disclosed in the '156 patent would not require dose adjustments in patients with any degree of renal impairment because the DPP-IV inhibitors are mainly excreted via the liver, and only to a minor extent via the kidney. (*See* the '156 patent, col. 23, ll. 1-10; Pajvani Decl. ¶ 35; *see also* Declaration of Dr. Pajvani in support of Plaintiffs' Opening Claim Construction Brief, ECF 349 at ¶ 16). However, the Court finds that the aforementioned additional features of claim 1, singly and in an ordered combination, recite a well-understood, routine, conventional activity, as recognized by the '156 patent, which do not transform the abstract idea of administering DPP-IV inhibitor to a patent eligible subject matter.

Accordingly, the Court finds that claim 1 of the '156 patent is patent ineligible under § 101 because claim 1 is directed to an abstract idea of administering a drug to a targeted patient population, and the additional claim limitations recited in claim 1 do not add "significantly more" to the aforementioned abstract idea in order to transform claim 1 into a patent eligible subject matter.

Claims 10-17 and 24-25 of the '156 Patent

Now, the Court focuses on claims 10-17 and 24-25 of the '156 patent, which Plaintiffs' assert against Defendants for infringement. As noted above, claims 10-17 are dependent claims that depend from independent claim 1. As a dependent claim, all the limitations of the claim to which it refers (i.e., claim 1) are incorporated by reference in the dependent claim. (*See* 35 U.S.C. 112(d), *supra* fn. 3). As such, for claims 10-17, which depend from claim 1, all the limitations of claim 1 are incorporated into claims 10-17, respectively. That is, claim 10, for example, recites,

> A method of treating and/or preventing metabolic diseases in a patient for whom metformin therapy is inappropriate due to at least one contraindication against metformin comprising
>
> orally administering to the patient a DPP-IV inhibitor wherein the contraindication is selected from the group consisting of: renal disease, renal impairment or renal dysfunction, unstable or acute congestive heart failure, acute or chronic metabolic acidosis, and hereditary galactose intolerance
>
> wherein the metabolic disorder is type 2 diabetes mellitus and wherein the contraindication is renal disease, renal impairment or renal dysfunction, and wherein said DPP-4 inhibitor is used for said patient in the same dose as for a patient with normal renal function.

(*see* col. 29, ll. 2-12; col. 31, ll. 55-60 of the '156 patent). The Court notes that the additional features added by claim 10 to claim 1 are limiting or further defining—(i) the metabolic disorder recited in claim 1 to type 2 diabetes mellitus; (ii) the contraindication recited in claim 1 to renal disease, renal impairment or renal dysfunction; and (iii) the dose of DPP-4 inhibitor for patients with normal renal functions. The Court notes that the "DPP-4 inhibitor" recited in claim 10 refers to the "DPP-IV inhibitor" recited in claim 1. The only difference being the Roman numeral annotation in claim 1.

The Court finds that these additional features recited in claim 10 are well-understood, routine, and conventional features that do not transform the abstract idea recited in claim 1 into a patent eligible subject matter. For example, the '156 patent recognizes that type 2 diabetes is a common disease associated with renal impairment and/or failure, and that remains inadequately treated, partly because of limitations in long term efficacy, tolerability and dosing inconvenience of existing antihyperglycemic therapies. (*See* the '156 patent, col. 1, ll. 15-30). The '156 patent also discloses that drugs belonging to the DPP-IV inhibitor class include, Sitagliptin, Vildagliptin, Saxagliptin and Alogliptin, and how their structural formulations can be modified in order to achieve a desired result for treating metabolic diseases such as type 2 diabetes. (*Id.* at col. 4, ll. 25—col. 9, ll. 30). As such, the Court notes that these additional features recite additional instructions that are well-understood, routine and conventional features in the art, as noted by the '156 patent, and that do not tie the abstract idea of claim 1 of 'administering' a drug to any tangible embodiments. Accordingly, the Court finds that the additional features recited in claim 10 do not transform the abstract idea recited in claim 1 into a patent eligible subject matter.

With respect to claims 11-17, the following additional features are added to claim 1—(i) the DPP-4 inhibitor and its major active metabolite(s) are primarily eliminated via hepatic metabolism or biliary excretion (claim 11); (ii) the DPP-4 inhibitor is excreted mainly via the liver (claim 12); (iii) excretion via the kidney represents a minor elimination pathway (claim 13); (iv) the DPP-4 inhibitor is excreted mainly unchanged (claim 14); (v) elimination via metabolism represents a minor elimination pathway (claim 15); (vi) the DPP-4 inhibitor has placebo-like safety/tolerability and/or is eliminated primarily as the parent drug via the liver (claim 16); and (vii) the main metabolite of the DPP-4 inhibitor is pharmacologically inactive (claim 17).

The Court finds that the additional features recited in claims 11-17 do not add "significantly more" to the abstract idea of claim 1. Instead, some of these additional features recite a natural phenomenon. For example, DPP-IV inhibitor being eliminated via hepatic metabolism, biliary excretion, or the liver; excretion via the kidney represents a minor elimination pathway, etc., represent a natural phenomenon of how the human body is interacting with the DPP-IV inhibitor that has been orally administered to a targeted patient population. *See Mayo*, 132 S.Ct. at 1296-97; *also see* Pajvani Decl. ¶ 22 (DPP-IV inhibitors, use of which is recited in claim 10-17 and 24-25, which are synthetic compounds, inhibit DPP-IV enzymes on the surface of the cells. This, in effect results in series of reactions in the human body to lower the blood glucose level in the body).

Accordingly, the Court finds that the additional features recited in claims 11-17 do not add "significantly more" to the abstract idea of claim 1. As such, claims 11-17 do not render claim 1 patent eligible under § 101.

Lastly, with respect to claims 24 and 25, the Court notes that these are additional independent claims, distinct from claim 1, as they do not relate back to another claim in their preamble. Claims 24 and 25, like claim 1, are method claims "of treating [type] 2 diabetes mellitus in a patient for whom metformin therapy is inappropriate". Upon review of claims 24 and 25, the Court notes that the aforementioned claims are similar to claim 1 in multiple respects. For example, claims 24 and 25 are—(i) method claims for treating a metabolic disease, such as type 2 diabetes; (ii) in a patient for whom metformin therapy is inappropriate because of a contraindication; (iii) by orally administering a DPP-IV inhibitor to the patient; and (iv) wherein the contraindication being, for example, renal disease, renal impairment, heart failure, etc.

The primary difference between claim 1 and claims 24 and 25 is the recitation of a particular DPP-IV inhibitor (i.e., BI 1356) in claims 24 and 25, which is not recited in claim 1.

The BI 1356 inhibitor is chemically represented as, 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine, which the '156 patent describes as a preferred embodiment of the DPP-IV inhibitors. (*See* col. 22, ll. 40-50 of the '156 patent). The BI 1356 is mainly excreted via the lever and only to a minor extent via the kidney. The non-renal elimination of the BI 1356 may be of significant benefit in a patient population that has a high prevalence of renal insufficiency and diabetic nephropathy. (*Id.* at col. 23, ll. 1-10).

The Court notes that claims 24 and 25, like claim 1, simply recite the act of 'administering' a particular DPP-IV inhibitor to a targeted patient population. Claims 24 and 25 do limit the scope of the claim to a particular DPP-IV inhibitor, BI 1356, which the disclosure of the '156 patent notes as being beneficial for patients with high prevalence of renal insufficiency and diabetic neuropathy. However, the Court notes that, at its core, claims 24 and 25 simply recite a single instruction of administering a drug to a targeted patient population, which is an abstract idea. *CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1371 (Fed. Cir. 2011) ("[M]ethods which can be performed mentally, or which are the equivalent of human mental work, are unpatentable abstract ideas...."). Lastly, like claim 1 as discussed above, the Court notes that the additional features recited in claims 24 and 25 do not add significantly more to the abstract idea of administering a DPP-IV inhibitor such that they transform the abstract idea into patent eligible subject matter. Accordingly, the Court finds that claims 24 and 25 are directed to patent ineligible subject matter under § 101.

Conclusion

For the foregoing reasons, because claims 10-17 and 24-25 of the '156 patent are directed to an abstract idea, the Court GRANTS Defendants' motion to dismiss under Rule 12(c).

s/Peter G. Sheridan
PETER G. SHERIDAN, U.S.D.J.

December 7, 2016